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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/357,675	CROCE, CARLO M.	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-24* is/are pending in the application.

4a) Of the above claim(s) *21-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 1/12/04 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Claim 17 (in part directed to fragments of 10 nucleotides) and claims 21-24 (entirely) are directed to an invention that is independent or distinct from the invention originally claimed for the reasons set forth in the Office action of 1/13/03.

Since applicant had received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 17 (in part, as directed to fragments) and claims 21-24 (entirely) remain withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicant's arguments filed 1/12/04 have been fully considered but they are not persuasive. Applicant believes that the filing of an RCE presents the opportunity to request reconsideration of the Restriction Requirement. The filing of an RCE does not provide Applicant the right to obtain examination of claims directed to an invention that is independent or distinct from the originally examined invention. MPEP 819. Applicant argues that the non-elected subject matter presents no additional search burden to the Office, and that it should already have been within the scope of the subject matter searched for sequences encoding a Nit1 protein. However, the search of the nucleotide sequence databases for those which encode a specific protein or are similar in sequence to a polynucleotide encoding a protein are carried out using quite different search parameters than a search for sequences comprising small oligomeric sequences in common with a reference nucleotide sequence. While the original search may or may not have revealed applicable prior art, it does not constitute a thorough search of the non-elected subject matter, which would require a new search using different search parameters. Furthermore, since the use of the oligomeric sequences differs substantially from that of the encoding sequences, a search for art which might make the non-elected invention obvious over a combination of references would also be required.

The amendment filed 1/12/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: recitation of "*NIT1* cDNA" in the amendment of the 'Brief Description" of Fig. 6 at page 6, lines 4-6. Fig. 6 labels these sequences as "NITD" not "*NIT1*".

Although the original description of Fig. 6 referred to *NIT1*, it made no sense in the context of what is shown in Fig. 6, and also did not identify the sequence as being a cDNA. The only other mention of Fig. 6 in the specification is at page 4, lines 14-16, which refers to it as "[Y]et another aspect of the present invention is a purified protein encoded by ... SEQ ID NO: 1 (Figure 6)," which does not identify the sequence as being that of *NIT1* nor of a cDNA. Page 6, lines 4-8, discuss *NIT1* genes, but make no reference to SEQ ID NO: 1. Applicant points to the original description of the figure as supporting the amendment. However, as indicated above this description made no sense in the context of Fig. 6, and it failed to indicate that it was a cDNA. Speculation by the Examiner that the sequence in Fig. 6 appeared to be a human sequence is not evidence supporting the changes, it is simply speculation. The Examiner cannot change the original written description in an application. Applicant is required to cancel the new matter in the reply to this Office Action. It is suggested that "*NIT1* cDNA" be replaced with –NITD--, as shown in Fig. 6, unless Applicant can provide evidence of an error in drafting the original specification that would support the amendment as being a correction.

Claim Objections

Claims 17-20 and 21-24 objected to because of the following informalities: The claims as presented in the amendment do not comply with 37 CFR 1.121, see 68 *Fed. Reg.* 38611 (June 30, 2003) or www.uspto.gov/web/patents/ifw/. Claims 17 and 18 should be identified as -- (previously presented) --, not "(previously added)" ; and claims 21-24 should be identified as -- (withdrawn) --, not "(previously added)". Appropriate correction is required.

Claim Rejections - 35 USC § 101 &112

Claims 17-20 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons of record set forth in the Office action of 1/13/03 (claim 17 was inadvertently omitted from the statement of rejection).

Claims 17-20 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments filed 1/12/04 have been fully considered but they are not persuasive. Applicant argues that a "strong relationship" has been established between Nit and Fhit, based upon the fusion of these two proteins in *C. elegans* and *D. melanogaster*, and the nearly identical tissue expression pattern of the separate proteins in mouse. The specification contains the speculation that there is a functional relationship between these two proteins, that they may act in concert or participate in the same enzymatic pathway. Applicant then makes a leap in logic that since Fhit had been identified as having a connection with human cancers, it is not expressed in a large fraction of certain types of cancer, that Nit would also correlate with cancer in humans. Applicant then asserts that the utility of Nit sequences for diagnosing and or screening for human cancer is established.

In response, the notion that Nit and Fhit are in some way involved in the same enzymatic pathway is simply speculation. No enzymatic pathway involving either protein had been identified at the time the invention was made, either in the prior art or in the specification. The

specification discloses that in humans, unlike in mouse, expression of Nit did not vary between different tissues (pages 13-14). Also, the expression pattern of Nit1 and Fhit was found to be nearly identical in mouse, but not in humans. Consequently, there is no evidence for a connection between these two proteins in humans, which raises doubt as to whether there is a connection in mouse. There is clearly insufficient evidence to "establish" such a connection, as asserted by Applicant.

Furthermore, the specification indicates that the apparent tumor suppressor activity of Fhit in cancer cell lines did not require Fhit enzymatic activity (page 3, lines 12-14). Consequently, even if Nit1 and Fhit are involved in a common enzymatic pathway, it would appear that the tumor suppressor activity Fhit may be separable from that enzymatic pathway. In which case, Nit1 would play no role in the tumor suppressor activity of Fhit. In addition, the specification (page 13, line 23-24) indicates that human Nit1 expression was tested in tumor cell lines and in normal adult tissues. No differences in expression were found. This situation contrasts significantly with Fhit, whose expression is absent in a large fraction of a variety of types of cancer. The specification fails to identify even a single type of cancer for which a change in Nit1 expression would be a characteristic. Consequently, if there is no difference in expression of Nit1 between normal tissue and cancer cells, there is no basis for using Nit1 expression as a marker for cancer diagnosis or screening. Since Nit1 mRNA is expressed in cancer cell lines, the protein would not appear to be absent in cancer cells, unlike Fhit. If Nit1 is not absent in cancer cells, one cannot argue that it is a tumor suppressor or even acts in concert with Fhit in tumor suppression. If it is not a tumor suppressor, then there is no basis for suggesting its use in cancer treament.

Finally, Applicant's contention that the connection between Fhit and cancer somehow establishes a connection between Nit1 and cancer, particularly when there is no hard evidence that Nit1 and Fhit have any functional connection in mammals, is simply speculation unsupported by unequivocal evidence. "Argument of counsel cannot take the place of evidence lacking in the record." *In re Scarbrough*, 182 USPQ 298, 302 (CCPA 1974).

Claims 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Recitation of "comprising" (claim 19) or "consisting of" (claim 20) "nucleotides 111 to 1086 of SEQ ID NO: 1" is new matter. Claims 19 and 20 were added by the amendment of 11/5/02. Applicant did not identify where the original specification supports DNA molecules comprising or consisting of less than the full length of SEQ ID NO: 1, as is Applicant's burden, see MPEP 714.02, last sentence of the third paragraph from the end and 2163.06 (I) last sentence. There does not appear to be any support for the limitation "nucleotides 111 to 1086 of SEQ ID NO: 1" for the minimum structure of a fragment of SEQ ID NO: 1 in the original specification. Page 4, lines 14-16, refer to a "protein encoded by a nucleic acid having a nucleotide sequence consisting of the coding region of SEQ ID NO: 1 (Figure 6)". However, the specification fails to identify that coding sequence of the protein. Fig. 6 shows seven different potential polypeptides (SEQ ID NO: 25-31), none of which are encoded by nucleotides 111 to

1086, although the coding sequence for SEQ ID NO: 25 includes this sequence. Thus, there is no evidence that such embodiments had been contemplated as being part of the originally disclosed invention, or were possessed by Applicant at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe
Primary Examiner
Art Unit 1632